Non-technical Abstract

Some ovarian cancer patients are incurable. All patients who die from this disease have been treated with standard forms of chemotherapy and radiation. The patients tumor cells have become resistant to drug and radiation therapy. We plan to genetically modify tumor cells from unrelated ovarian cancer patients, which have been adapted to cell culture, to increase the tumor's susceptibility to one form of chemotherapy. In addition, we plan to injected these tumor cells with increased sensitivity to chemotherapy into the patients' existing tumor in order to transfer the susceptibility to chemotherapy to the patients' tumor cells which cannot be genetically modified in tissue culture.

The gene for herpes simplex virus thymidine kinase (TK) will be inserted into the unrelated ovarian tumor cells to increase their susceptibility to the drug ganciclovir. We have demonstrated that tumor cells containing the HSV-TK gene will be killed by the drug ganciclovir both in tissue culture and in mice. In addition, we have shown that TK containig irradiated tumor cells can transfer the susceptibility to ganciclovir to nearby unmodified TK negaktive tumor cells. Thus, we plan to inject irradiated TK positive ovarian tumor cells into the tumor containing abdomen of ovarian cancer patients in relapse (with no cure). The TK tumor cells will then be treated with ganciclovir to activate the TK positive tumor cells such that both the TK positive and TK negative tumor dies.